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| EXAMINER | |
|---|---|
| EPPERSON, JON D | |
| ART UNIT | PAPER NUMBER |
| 1639 | |

DATE MAILED: 01/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/836,145 | CRAVATT ET AL. | |
| | Examiner | Art Unit | |
| | Jon D Epperson | 1639 | |

*-- Th MAILING DATE of this communication app ars on the cov r sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *12,14,16-18 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,14,16-18 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/2/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Request for Continued Examination (RCE)*

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection (e.g., see 10/12/04 Response). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/12/04 has been entered. Claims 1-24 were pending. Applicants canceled claims 1-11, 13, 15, 19-20 and newly added claim 25 (claim 25 was added in the 7/12/04 Response). No claims were added and claims 12 and 14 are currently amended. Therefore, claims 12, 14, 16-18 and 21-24 are currently pending. An action on the merit follows.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

### Withdrawn Objections/Rejections

2. The Enablement and Written Description Rejections under 35 U.S.C. § 112, first paragraph are withdrawn in view of Applicants' arguments and/or amendments. All other rejections are maintained and the arguments are addressed below.

### Outstanding Objections and/or Rejections

#### *Claims Rejections - 35 U.S.C. 102*

3. Claims 12, 14, 16, 17 and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Purohit et al. (Purohit, A.; Williams, G. J.; Howarth, N. M.; Potter, B. V. L.; Reed, M. J. "Inactivation of Steroid Sulfatase by an Active Site-Directed Inhibitor, Estrone-3-O-Sulfamate" *Biochemistry* **1995**, *34*, 11508-11514) as evidenced by Luppa et al. (Luppa, P.; Hauck, S.; Schwab, I.; Birkmayer, C.; Hauptmann, H. "6α-Biotinylated Estrone: Novel Tracer in Competitive Chemiluminescence Immunoassay of Estrone in Serum" *Clin. Chem.* **1995**, *41(4)*, 564-570) and as evidenced by Alcock (Alcock, S. "SENSPOL: European Network on Sensors for Monitoring Water Pollution" *European Union Thematic Network Newsletter* **2002**, *6*, 1-29). Please note: MPEP 2131.01(d) permits the citation of references or evidence in an anticipation rejection under 35 U.S.C. § 102 in order to show that a characteristic not disclosed in the reference is inherent.

For ***claims 12 and 14***, Purohit et al. (see entire document) disclose a method for screening a library of estrones for potential inhibition of sulfatase enzymes (i.e., estrone sulfatase and dehydroepiandrosterone sulfatase react with and thus inhibit the "active site" of the enzyme) in placental microsomes and intact MCF-7 breast cancer cells (e.g., see Purohit et al., abstract; see also figure 1, compounds 4-6), which anticipates claims 12 and 14. Here, the combinatorial chemical library has the same formula as that disclosed by Applicants wherein the X group is "estrone", the L group is a "bond", the F group is "$SO_2$" or alternatively "$SO_2N$" and the R group varies in the library to include "$NH_2$, NHMe and $NMe_2$" or alternatively "H or Me" (e.g., see Purohit et al., figure 1, compounds 4-6, especially compound 6 wherein R is alkyl).

Furthermore, Purohit et al. disclose combining members of the library with a complex mixture (e.g., the placental microsomes and intact MCF-7 breast cancer cells that contain estrone sulfatase and dehydroepiandrosterone sulfatase) wherein conjugates are formed between the library members and the sulfatase proteins (see Purohit et al., page 11513, figure 8; see also Materials and Methods section). In addition, Purohit et al. disclose isolating said conjugates from the active and inactive complex mixture (e.g., see Purohit et al., page 11509, column 2, paragraph 1). Finally, Purohit et al. disclose comparing both "active" and "inactive" reaction mixtures (see Purohit et al., abstract, "The enzyme [sulfatase] is protected from inactivation by estrone sulfate [i.e., active form], which is also consistent with active site-directed inhibition. EMATE is proposed to inactivate estrone sulfatase by irreversible sulfamoylation of the enzyme [i.e., inactive form]"; see also page 11512, figure 6). Furthermore, Purohit et al. disclose using two separate "portions" for the active and inactive mixture i.e., a "portion" with estrone sulfate added and a "portion" without any estrone sulfate added (see Purohit et al., page 11510, column 1, paragraph 1).

For newly amended claims 12 and 14, Purohit et al. do not explicitly state that the estrone portion of the molecule has the ability to act as a "hapten" i.e., has the ability to elicit an immune response (e.g., see newly amended claims 12 and 14 wherein "X is a ligand selected from a group consisting of ... and hapten"). However, the Examiner contends that the estrone disclosed in Purohit et al. would inherently possess this activity as evidenced by Luppa et al. and Alcock (e.g., see Luppa et al., abstract which shows that estrone can act as a hapten for use in competitive chemiluminescence immunoassays for

estrone in serum; compare also compound Bio-E1 in figure 1 of Luppa et al. to compounds (1)-(6) in figure 1 of Purohit et al.; see also figures in Luppa et al.; see also Alcock, page 16, "Spotted transducer" section wherein estrone is again disclosed as a hapten, "... each polymer-hapten conjugate (atrazine, estrone and isoproturon [are the haptens]) ..."). If the prior art structure is capable of performing the intended use, then it meets the claim. The Office does not have the facilities to make a comparison and the burden is on the applicants to establish any difference between the transducing elements of the art and the instant claims. Se In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ 2d 1922 1923 (PTO Bd. Pat. App. & Int.). Here, both Luppa et al. and Alcock clearly demonstrate that estrone has the capability of performing the intended use (i.e., ability to act as a hapten).

For ***claim 16***, Purohit et al. disclose library members with different on-rates (see page 11510, Results, "Nature of EMATE Inhibition of Sulfatase Activity" section, especially column 2, paragraph 4).

For ***claim 17***, Purohit et al. disclose estrone, which falls within the category of hapten (e.g., see above)

For ***claim 21***, Purohit et al. disclose F = sulfamate (see Purohit et al., page 11508, figure 1, compound 6).

***Response***

4. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified

from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

**[1]** Applicants argue, "As previously discussed, Purohit et al. fail to teach using a combinatorial chemical library which includes a plurality of compounds. The Examiner has stated that compounds (4)-(6) illustrated by Figure 1 ... represent a combinatorial library. The Applicants respectfully disagree. There is nothing in Purohit et al. describing the compounds (4)-(6) ... as a library, i.e., while being mixed together. Thus, a "plurality of members" limitation recited in each of claims 12 and 14 is not taught" (e.g., see 10/12/04 Response, page 12, section C).

**[2]** Applicants argue, "... claims 12 and 14 recite a number of ligands X. None of these ligands can be found in Purohit et al. who only teach using estrone derivatives" (e.g., see 10/12/04 Response, page 12, section C).

This is not found persuasive for the following reasons:

**[1]** In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., library members "being mixed together" at the same time presumably in the same reaction vessel) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, nothing in Applicants' claims preclude the possibility of parallel screening each library member in a separate reaction wherein the library members are not "mixed together" in the same reaction vessel i.e., step (1) of the

claims does not state, "combining with said complex mixtures of proteins, in an active form and an inactivated form, said combinatorial chemical library [in the same container] ... ."

Furthermore, claims are to be given their broadest reasonable interpretation consistent with Applicants' specification (e.g., see *In re Zletz*, 13 USPQ2d 1320, 1322 (Fed Cir. 1989) (holding that claims must be interpreted as broadly as their terms reasonably allow); MPEP § 2111. Here, nothing in Applicants' specification precludes the possibility of using a library wherein the library members are not mixed together (e.g., parallel screening in separate vessels or sequential screening in separate vessels). It is also noted that the term "library" is used quite broadly in the art to mean "any ensemble of molecules" (e.g., see Janda, K. D. "Tagged versus untagged libraries: Methods for the generation and screening of combinatorial chemical libraries" PNAS USA November **1994**, 91, 10779-10785, especially page 10779, column 1, last sentence, "In its purest form, a combinatorial chemical library can be defined as ***any ensemble of molecules***"). As Applicants have not pointed to any definition in the specification for the term "library", the Examiner contends that "any ensemble" of molecules that reads on those set forth in the claims is deemed to be a library. Consequently, the "ensemble" of molecules shown in figure 1 of the Purohit et al. reference clearly falls within the definition of a library.

**[2]** The Examiner contends that estrone falls within the definition of a "hapten" as outlined in the newly amended rejection above. Thus, the claim is anticipated.

Accordingly, the 35 U.S.C. § 102 rejection cited above is hereby maintained.

***Claim Rejections - 35 USC § 103***

5. Claims 12, 14, 16-18 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gygi et al. (Gygi, S. P.; Rist, B.; Gerber, S. A. Turecek, F.; Gelb, M. H.; Aebersold, R. "Quantitative analysis of complex protein mixtures using isotope-coded affinity tags" *Nature Biotechnology* **1999,** 17, 10, 994-999) and Liu et al. (Liu, Y.; Patricelli, M. P.; Cravatt, B. F. "Activity-based protein profiling: The serine hydrolases" *PNAS* **1999**, 96, 26, 14694-14699) (IDS #6) and Bogyo et al. (Bogyo, M.; McMaster, J. S.; Gaczynska, M.; Tortorella, D.; Goldberg, A. L.; Ploegh, H. "Covalent modification of the active site threonine of proteasomal β subunits and the *Escherichia coli* homolog HSIV by a new class of inhibitors" *PNAS* **1996**, 94, 6629-6634).

For ***claims 12, 14, 16-18 and 21-24*** Gygi et al. disclosed a method for quantitative analysis of complex protein mixtures using isotope-coded affinity tags (ICAT) (Abstract; pg. 994, right col., 6-9). The method comprises of the following steps: (1) The side chains of cysteinyl residues in a reduced protein sample representing one cell state are derivatized with the isotopically light form of the ICAT reagent. The equivalent groups in a sample representing a second cell state are derivatized with the isotopically heavy reagent (refers to the combining step). (2) The two samples are combined and enzymatically cleaved to generate peptide fragments (refers to the sequestering step). (3) The tagged peptides are isolated by avidin affinity chromatography (refers to the determining step). (4) Finally, the isolated peptides are separated and analyzed by LC-MS/MS (electrospray ionization (ESI) MS/MS, in conjunction with microcapillary liquid chromatography (LC)) (pg. 994, right col., 12-24; figure 2) (refers to the comparing step).

The method of Gygi et al. does not expressly disclose that the probe can contain the structures disclosed by Applicants wherein F is a "sulfonyl group" and the targets are the "active site" regions of serine hydrolases.

The combined teachings of Liu et al. and Bogyo disclosed a method of activity-based protein profiling using an "active site" directed probe (e.g., see Liu et al., abstract). The probe disclosed by Liu et al. is a biotinylated fluorophosphonate, FP-biotin, (pg. 14694, left col., lines 30-33), but Bogyo et al. disclose that the "sulfonyl groups" can also be used as probes (e.g., see Liu et al., page 14699, column 1, paragraph 2, "Although we have demonstrated the utility of a biotinylated fluorophosphonate as a rapid and high-sensitivity probe for detecting serine hydrolase activities directly from crude cell and tissue samples, one could envision that additional types of tagged irreversible inhibitors may succeed at labeling other classes of enzymes. For example, Bogyo and colleagues have recently used radiolabeled vinyl sulfones as selective reagents for marking members of the proteasome family of proteases (36) [wherein reference 36 refers to the Bogyo et al. reference]"). The method steps of reacting protein samples (proteomic mixture) with FP-biotin (activity-based probe) include combining FP-biotin mixture with the protein samples and detecting the FP-biotin-reactive proteins by SDS/PAGE-Western Blotting (pg. 14695, right col., lines 26-64). The FP-biotin-reactive proteins are further analyzed by MALDI mass spectrometry (pg. 14696, left col., lines 11-15). FP-biotin can react with numerous serine hydrolyses (target enzyme) in crude cell and tissue samples (pg. 14698, left col., lines 1-8). Finally, the combined teachings of Liu et al. and Bogyo et al. disclose combining said library with both "active" and "inactive" proteins (e.g., see Liu et

al., page 14696, column 2, paragraph 2 wherein the active FAAH and the inactive S241A are disclosed; see also last full paragraph wherein active (inhibitor free) and inactive (inhibitor bound) serine proteases are disclosed; see also Liu et al., page 14695, column 2, middle paragraph, wherein inactivation of active proteins was caused by "heating" to create inactive proteins).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use the biotinylated sulfones linked by N-(5-pentylamine)-decanamido probes as taught by the combined teachings of Liu et al. and Bogyo et al. in the method of Gygi et al. because Bogyo et al., Gygi et al. and Liu et al. disclose methods of detecting proteins from a crude cell samples (Gygi: pg. 994, right col., 6-9, and pg. 995, fig. 2; Liu: pg. 14698, left col., lines 1-8) (i.e., the references represent analogous art). One of ordinary skill in the art would have been motivated to include that the biotinylated sulfone probes and the target proteins disclosed by the combined teachings of Liu et al. and Bogyo et al. (e.g., serine hydrolases) in the method of Gygi et al. for the advantage of providing a probe that is specific for profiling in a single class of proteins (Liu: pg. 14694, lines 30-33) since both Gygi et al. and Liu et al. disclose method of detecting proteins from a crude cell samples (Gygi: pg. 994, right col., 6-9, and pg. 995, fig. 2; Liu: pg. 14698, left col., lines 1-8). Furthermore, a person of skill in the art would have been motivated to combine the Bogyo et al. and Liu et al. references because Liu et al. explicitly states that these two references should be combined (see Liu et al., page 14699, column 1, paragraph 2, "Although we have demonstrated the utility of a biotinylated fluorophosphonate as a rapid and high-sensitivity probe for detecting serine

hydrolase activities directly from crude cell and tissue samples, one could envision that additional types of tagged irreversible inhibitors may succeed at labeling other classes of enzymes. For example, Bogyo and colleagues have recently used radiolabeled vinyl sulfones as selective reagents for marking members of the proteasome family of proteases (36) [wherein reference (36) refers to the Bogyo et al. reference]").

***Response***

6. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

**[1]** Applicants argue, "Gygi et al. fail to teach a combinatorial chemical library wherein "members of said combinatorial chemical library react with an active site of said protein member" (e.g., see 10/12/04 Response, page 13, paragraphs 1 and 3).

**[2]** Applicants argue, "Gygi et al. fail to teach that 'inactivated complex mixtures are comprised only of active proteins.' Instead, the protein mixture described in Gygi includes only denatured proteins the activity of which have been destroyed" (e.g., see 10/12/04 Response, page 13, paragraph 2-3).

**[3]** Applicants argue, "... that Liu et al. is not available as a prior art reference ... since the subject matter set forth in Liu et al. was derived from ... Applicants' own work" (e.g., see 10/12/04 Response, page 13, last paragraph).

This is not found persuasive for the following reasons:

**[1]** In response to applicant's arguments against the Gygi et al. reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). For example, please note that the "combined teachings" of Gygi et al. Liu et al. and Boygo et al. teach the use of a library wherein members of said combinatorial library react with an active site of a protein (e.g., see Liu et al., abstract wherein library members that inhibit the "active site" of serine hydrolases are disclosed).

**[2]** In response to applicant's arguments against the Gygi et al. reference individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). For example, the "combined teachings" of Gygi et al., Liu et al. and Bogyo et al. disclose combining said library with both "active" and "inactive" proteins (e.g., see Liu et al., page 14696, column 2, paragraph 2 wherein the active FAAH and the inactive S241A are disclosed; see also last full paragraph wherein active (inhibitor free) and inactive (inhibitor bound) serine proteases are disclosed; see also Liu et al., page 14695, column 2, middle paragraph, wherein inactivation of active proteins was caused by "heating" to create inactive proteins).

**[3]** The Examiner agrees with Applicants assessment of MPEP 716.10, example 2. However, the 37 CFR § 1.132 declaration is defective because it refers to the wrong U.S. Patent Application Serial No. (e.g., see 1/12/04 Declaration under 37 CFR § 1.132, section 1, "I am a

co-inventor ... in U.S. Patent Application Serial No. 09/738,954", which is incorrect because the current application is 09/836,145). Thus, Applicants arguments are moot.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

## New Objections and/or Rejections

### *Objections to the Claims*

7. Claims 17 and 24 are objected to because of the following informalities:

A. Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Here, the Markush listing recited in claim 17 includes members not recited in the broader independent claim (e.g., vicinal diol, Fluorescein, a peptide, etc).

B. Claim 24 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Here, the Markush listing recited in claim 24 includes members not recited in the broader independent claim (e.g., compound 9 represents a "quinoline" that is not recited in the independent claim).

***Claim Rejections - 35 U.S.C. 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 12, 14, 16-18 and 21-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claims 12 and 14**, the term "a peptide of polypeptide" is vague and indefinite. For example, it is not clear how the peptide could come from anything other than a polypeptide? Thus, the additional words "of polypeptide" only serve to confuse a term (i.e., peptide) that would otherwise have a clear definition. Applicants are requested to clarify and/or correct. Therefore, claims 12, 14 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. ***Claim 24*** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language. Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993) (citations omitted). Reference

characters corresponding to elements recited in the detailed description and the drawings may be used in conjunction with the recitation of the same element or group of elements in the claims. See MPEP § 608.01(m). Here, Applicants have failed to incorporate the chemical structures of sulfonates 1-11 and 15-17 disclosed, for example, in figure 10 of the specification. The compounds could be easily incorporated into the claim and, as a result, no such "exceptional circumstances" exist. See MPEP § 2173.05(s). In addition, it is not clear what sulfonates 15-17 refer to in the claim.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
January 16, 2005